REMARKS

Claims 1-7 are currently pending in the application. Claims 4-7 are withdrawn. Claims 1-3 have been amended. Support for the amendments may be found throughout the specification as filed. No new matter has been added.

Amendment of the claims should in no way be construed as acquiescence to any of the Examiner's rejections. The amendments of claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in any way. Applicants reserve the right to further prosecute the same or similar claims in the instant application, or in a divisional or continuation patent application.

Objection to the claims

Claim 2 is objected to because the word "malignat" is misspelled. Claim 2 has been amended to omit the misspelled word. Applicants believe that the amendment renders moot the objection.

Rejection of claims 1-3 under 35 U.S.C. § 112, second paragraph

Claims 1-3 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. More specifically, the Examiner states:

> The term "malignant potential" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. (See *Office Action* at p. 3.)

Applicants have amended claim 1 to recite a method for detecting in vitro human gastric carcinoma progressing from human gastric dysplasia. Claims 2 and 3 have been amended to provide proper antecedent basis. More specifically, claims 2 and 3 have been amended to recite "[t]he method of claim 1 . . ." and "[t]he method of claim 2 . . ." respectively, in lieu of reciting an in vitro detection of malignant potential of dysplasia. Applicants believe that the amendment renders these claims definite, thereby obviating this rejection. Reconsideration is respectfully requested.

In support of this rejection, the Examiner further states:

> The limitation (e.g. claim 1) that the procedure involve "extraction of genomic DNA from cells in a sample of tissue or body liquids" is not considered to meet the requirements of positive process steps because, since the claim is written in the passive tense, no guidance is given as to how to extract the DNA. (See *Office Action* at pp. 3-4.)

Applicants have amended claim 1 to recite that the method comprises, "extracting genomic DNA . . .; detecting the methylation state . . .; and evaluating the risk of gastric carcinoma . . . ." Applicants believe that amended claim 1 complies with the requirement in reciting positive process steps, thereby obviating the rejection of this claim and claims 2 and 3, which depend therefrom. Reconsideration is respectfully requested.

Rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph

Claims 1-3 stand further rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. More specifically, the Examiner states:

> In the instant case, the specification teaches sequences for identifying human p16 methylation. However, the claims read on a sample from any organism, and yet the specification does not provide any sequence information for non-human organisms. (See *Office Action* at p. 5.)

Applicants have amended claim 1 to recite a method and steps for detecting in vitro human gastric carcinoma progressing from human gastric dysplasia. Applicants believe that the amendment obviates the rejection of this claim and claims 2 and 3, which depend therefrom. Reconsideration is respectfully requested.

Claims 1-3 stand further rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. More specifically, the Examiner states:

> Given the lack of data from all organisms, the lack of significant data from gastric tissue, the lack of definition for malignant potential, and the lack fo study from other tissues, a method of in vitro detection of malignant potential of dysplasia comprising extracting genomic DNA from any sample, detecting the methylation state of p16 CpG islands in genomic DNA by amplification; and detemining malignant potential of any sample based upon the presence of methylated p16 CpG is replete with unpredictable experimentation that is considered undue. (See *Office Action* at p. 14.)

Applicants have amended claim 1 to recite a method for detecting in vitro human gastric carcinoma progressing from human gastric dysplasia. The steps comprise (a) extracting genomic DNA from a sample comprising human gastric dysplasia cells; (b) detecting the methylation state of *p16* CpG islands in the genomic DNA; and (c) evaluating the risk of gastric carcinoma based upon the presence of methylated *p16* CpG islands. Applicants believe that the amendments to claim 1 obviate the rejection of this claim and claims 2 and 3, which depend therefrom. Reconsideration is respectfully requested.

Rejection of claims 1-3 under 35 U.S.C. § 102

Claims 1-3 stand rejected under 35 U.S.C. § 102, for allegedly lacking novelty over each of Wong et al., Bai et al., and Belinsky et al. With respect to Wong et al., the Examiner alleges, in part, that because Wong et al. teaches detecting p16 methylation in the plasma or serum of HCC (hepatocellular), Wong et al. anticipates the claims. With respect to Bai et al., the Examiner alleges, in part, that because Bai et al. teaches observation of p16 promoter hypermethylation during the process of neoplastic progression in rat gastric carcinoma, Bai et al. anticipates the claims. With respect to Belinsky et al., the Examiner alleges, in part, that because Belinsky teaches a molecular marker-based method for monitoring and detecting cancer in humans by detecting the aberrant methylation of the p16 gene from sputum samples, Belinsky et al. anticipates the claims. (See *Office Action* at pp. 15-16.)

Applicants respectfully traverse. Applicants' specification states on page 13, lines 3-10:

> The present assay can specifically predict the malignant potential of gastric dysplasia. Aberrant *p16* methylation was not observed in any samples of dysplasia that did not progress (Specificity, 100%). The sensitivity for detection of malignant potential of all samples of dysplasia that progressed to gastric carcinomas is only 24%. However, the sensitivity for detection of malignant potential of these samples of *p16*-methylated dysplasia is very high, because all 5 patients with *p16*-methylated gastric dysplasia progressed to gastric carcinomas at the sampling sites of their stomachs within the following five years (Sensitivity, 100%).

Thus, the instant specification teaches that of a sampling of patients with methylated p16 CpG islands in gastric dysplasia, all such patients with *p16*-methylated gastric dysplasia after 5 years progressed to gastric carcinoma (100% sensitivity). Thus, applicants found a correlation of

p16 methylation in gastric dysplasias and their progression to gastric carcinoma. Such correlation is not taught or suggested in the art.

It is Applicants who for the first time teach a method for detecting in vitro human gastric carcinoma progressing from human gastric dysplasia as recited in amended claims 1-3. therefore, Applicants' amended claims are not taught or suggested by the cited art. Accordingly, reconsideration is respectfully requested.

CONCLUSION

If a telephone conversation with Applicants' Agent would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1749. no fees are believed to be due; however, the Commissioner is hereby authorized to charge any necessary fees to our **Deposit Account No. 06-1448, Reference CNL-700.01**.

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Respectfully submitted,

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